> ***"We know from drug toxicity studies that animal tests are very imperfect indicators of human toxicity: only clinical experience and careful control of the introduction of new drugs can tell us about their real dangers."***
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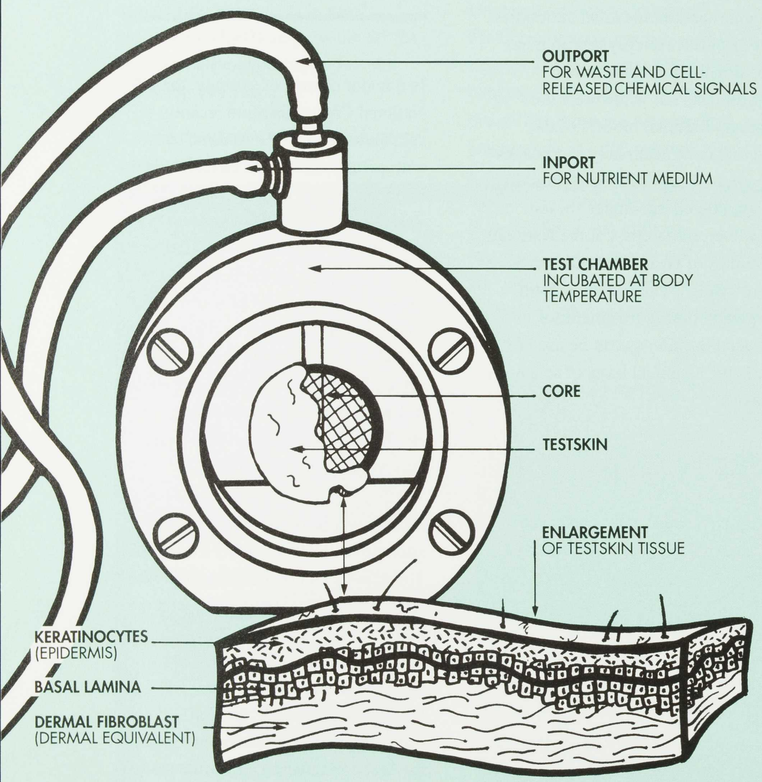
> ***Lancet*, April 22, 1972**

tests carried out at Denmark's Roskilde University Center, the lethal concentration of chemicals to cultures of human blood lymphocytes showed "very good correlation" with their reported lethal doses in people.[10] The lymphocytes were obtained from a volunteer's blood sample.

In a welcome initiative, companies are now marketing human tissue tests to predict adverse drug effects on specific organs. The La Jolla-based company Marrow-Tech Inc. in California recently introduced complete culture systems for human bone marrow, liver, oral mucosa and skin for *in vitro* safety evaluation. In the case of the human skin model, the different layers of cells which form normal skin are placed in layers on a nylon mesh, producing a full-thickness skin equivalent.



"Epipack," from the Clonetics Corporation of San Diego, contains live normal cloned human skin cells. The test assesses irritancy and absorption without using animals.

Sophisticated computer programs are now helping to design new medicines and assess the safety of chemicals. Drug discovery has been a hit and miss affair with 7,000-8,000 substances tested for every one that reaches the market. Now a more rational approach is possible: based on the idea that drugs must be the right shape to trigger their effects, computer scientists are using 3-D computer graphics to design new treatments.

The New York company Health Designs Inc. has developed computer programs to predict toxicity on the basis of chemical structure. A high level of accuracy is achieved when results are compared with the outcome of animal experiments, but the method would be more relevant if the computer were programmed with human rather than animal test data.

One of the most important advances over the past 20 years is the development of rapid *in vitro* tests to identify cancer-causing chemicals. Continued reliance on tediously slow animal experiments poses a threat to our health because they are unable to tackle the thousands of untested chemicals currently in use.

With individual tests costing $1 million and taking 3-8 years to complete, the National Toxicology Program has estimated that if animals were used, it would take an additional 80 years to study all existing chemicals. In the meantime, the further 500 new substances introduced every year would result in a backlog of 40,000 untested chemicals. Furthermore, their very expense mitigates against re-testing should results be less than clear cut.

On the other hand, *in vitro* tests with cells, bacteria and yeasts, together with computer simulation methods, take only days to perform which at least makes it possible to tackle the problem.

ESSENTIAL drugs

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The realization that animal tests are an unsafe guide to drug safety, should limit the introduction of new medicines to those for which there is a medical need, so that hazards can be minimized. Yet an analysis by health economist Etienne Barral found that 70% of new medicines introduced onto the world market between 1975 and 1984 offered no therapeutic improvement over existing products.[1] This is confirmed in a report commissioned by the US Agency for International Development:[2] "As many as 70% of the pharmaceuticals in the world today represent duplicative, 'me-too' or non-essential products. Many are minor variations on a prototype drug and offer no therapeutic advantage. Other drugs represent suboptimal choices of treatment because of high toxicity relative to the therapeutic benefit."

"Me-too" drugs have no real medical worth and are developed for commercial reasons to ensure a patented product stays on the market. Nevertheless they may confuse doctors faced with a choice of drugs all doing the same thing. In March, 1987 Britain's *Drug & Therapeutics Bulletin* noted that "the existence of many apparently similar preparations seldom increases therapeutic options, but greatly increases the risk of unwanted effects and makes them more difficult to detect." The *Bulletin* argued that the use of a smaller number of medicines should increase knowledge of their real benefits and hazards so leading to safer prescribing.

Sidney Wolfe, Director of the Public Citizen Health Research Group, believes that legislation should require new drugs to have an advantage in safety or efficacy over existing products, thereby enabling the FDA to focus more of its resources on important treatment.[3] Wolfe notes that the drugs recently withdrawn on safety grounds from the US market, including Oraflex, Zomax, Suprol, Merital and Selacryn, were not important advances over already available medicines. In Norway, drugs can only be introduced if there is judged to be a medical *need* for them.

Developing an essential drugs policy along these lines would not only benefit patients but substantially reduce the number of animal experiments.